

### **Remarks/Arguments**

Claims 1-11 and 16-23 are pending in the application, claim 12 having previously been canceled. Claims 16-21 have been withdrawn from consideration. Claims 1-15 and 22-23 have been rejected.

### ***Claim Rejections – 35 USC §102***

Claims 1, 2, 5, 6, 8, 10, 11, 22 and 23 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. 5,824,638 to Burnside *et al.* As stated in the previous response, Burnside discloses compositions comprising water-in-oil emulsions, whereas the present invention comprises oil-in-water emulsions. This distinction should not be overlooked, because whether an emulsion is prepared as a water-in-oil emulsion or an oil-in-water emulsion depends on the volume fraction of both phases—and on the type of emulsifier chosen. In the present case, the inventors have discovered that linoleic acid does not act in the solubilizing composition as one would have expected it to, especially given the disclosures by others such as Burnside that linoleic acid is a lipophilic/hydrophobic compound. When the inventors tried to replace linoleic acid in the present composition with other lipophilic compounds such as other free fatty acids, triglycerides, monoglycerides, soy oil, corn oil, canola oil, docosahexanoic acid, etc., the emulsion was less stable. Presumably, because additional lipophilic/hydrophobic material had been added, more TPGS would have been needed to act as a surfactant and stabilize the emulsion. In the present case, however, the amount of TPGS needed to stabilize the emulsion can actually be decreased if TPGS is used in combination with linoleic acid. What is being emulsified is a lipophilic component, and what is being formed is an oil-in-water emulsion. To one of skill in the art, it would have made better

sense to add a sufficient amount of TPGS and/or TPGS and an additional surfactant/emulsifier in order to emulsify a hydrophobic component such as alpha-tocopherol, gamma-tocopherol, coenzyme Q10, etc., rather than to add an additional component that is generally considered to be used for the hydrophobic portion of a water-in-oil emulsion, as described by Burnside.

In Example 1, Burnside describes the use of Pluronic<sup>®</sup> L44. In Examples 3, 4, 5, 6, 7, 9, 13, 15, 17, 18, and 19, Pluronic<sup>®</sup> (Poloxamer) is used as an added emulsifier. In Examples 8, 10, 11, 12, 17, and 19, Tween<sup>®</sup> is used as an emulsifier.

Claims 1, 2, 5, 6, 7, 8, 10, 11, 22 and 23 have also been rejected under 35 U.S.C. 102(b) as anticipated by WO 99/29300 (Mishra *et al.*). As was disclosed by Burnside, however, Mishra also uses detergent surfactants. For example, Example 1 discloses the use of 200 mg Tween<sup>®</sup> 80 in combination with 130 mg linoleic acid and 108 mg vitamin E TPGS. In Example 2, 375 mg Tween<sup>®</sup> 80 was used, while only 130 mg linoleic acid and 76 mg vitamin E TPGS were included in the composition. Other compositions disclosed by Mishra include Tween<sup>®</sup> 80 and/or Tween<sup>®</sup> 40.

Surfactants are generally irritating to membranes, making them less desirable components of pharmaceutical and nutraceutical formulations. Discovering that linoleic acid can act as a co-surfactant with TPGS allows formulation of oil-in-water emulsions to provide aqueous formulations of oil-soluble vitamins such as vitamin E, without necessitating the use of irritating compounds generally classed as surfactants.

The examiner has stated that "it cannot be said that the inclusion of a surfactant, detergent or emulsifier detracts from or otherwise changes the novel characteristics of the invention." Applicant respectfully traverses, as it is clear to those of skill in the art

that the ability to formulate without the addition of common surfactants is novel and needed.

Applicant respectfully requests that the amendment to claim 1 be admitted for consideration. Support for the amendment to include the phrase "effective for solubilizing a lipophile in an aqueous emulsion" may be found in the specification (see, for example, page 3, lines 15-17).

### ***Claim Rejections – 35 U.S.C. §103***

Claims 3, 4, 9 and 13-15 were also rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. 5,824,638 to Burnside *et al.* in view of U.S. 5,883,103 to Burnside *et al.*, WO/29300 to Mishra *et al.*, and Roy *et al.* (FEBS Lett.). Roy teaches one of the benefits of vitamin E, while the teachings of Burnside and Mishra have been discussed above.

Applicants again submit that both Burnside and Mishra provide disclosures that would indicate to one of skill in the art that compositions of the present invention would not be effective in the absence of a surfactant/detergent such as Tween<sup>®</sup> or Pluronic<sup>®</sup>. As stated previously, other hydrophobic/lipophilic compounds destabilized the emulsions. Burnside and Mishra do not distinguish linoleic acid sufficiently from other hydrophobic/lipophilic agents to provide a motivation to one of skill in the art to utilize it in the absence of surfactant/detergent to form oil-in-water emulsions.

The oil-in-water emulsions of the invention provide a way to increase delivery of fat-soluble vitamins to individuals who have difficulty absorbing those vitamins. Many such individuals suffer from conditions that might be exacerbated by the inclusion of commercial surfactants in the vitamin preparation (e.g., Crohn's disease, cystic fibrosis).

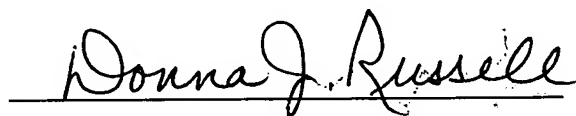
The difficulty encountered by those skilled in the art of formulation has been the preparation of an emulsion such as that described by the inventors without the addition of surfactants, which can be irritating to human/animal membranes.

Respectfully submitted,

A handwritten signature in cursive script that reads "Donna J. Russell".

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I hereby certify that this correspondence is being deposited with the United States Postal service with sufficient postage as first-class mail in an envelope addressed to Mail Stop RCE, Commissioner for Patents, USPTO, P.O. Box 1450, Alexandria, VA 22313-1450, on December 24, 2008.

A handwritten signature in cursive script that reads "Donna J. Russell", positioned above a horizontal line.